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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/893,344 | 06/28/2001 | Michal Eisenbach-Schwartz | EIS-SCHWARTZ=21 | 1157 |

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| EXAMINER | |
|---|---|
| NICHOLS, CHRISTOPHER J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1647 | 6 |

DATE MAILED: 01/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/893,344 | EISENBACH-SCHWARTZ ET AL. | |
| | Examiner | Art Unit | |
| | Christopher Nichols, Ph.D. | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *10-13 and 16-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 June 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of Group I Claims 1-9 and 14-15 drawn to a method of treating glaucoma via administration of poly-Glu,Tyr peptide in Paper No. 5 (23 October 2002) is acknowledged. The traversal is on the ground(s) that a search of poly-Glu,Tyr would cover both groups I and II. This is not found persuasive because Group I is drawn to a method using a therapeutic peptide, classified in class 514, subclass 2 and Group II is drawn to a method of using cells in a therapy, classified in class 435, subclass 455. In addition, the search for Group I would only entail therapeutic peptides not cell transplantation therapy. Also, a search of Group II would cover the art of therapeutic cell administration that is not co-extensive with therapeutic peptides. Therefore, Group I and Group II being in separate classifications and different arts, are not linked as to share a common search.

2. Newly submitted claims 16-31 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 16-31 are drawn to a pharmaceutical composition of poly-Gly,Tyr (also known as pEY or $pE^{50}Y^{50}$). Inventions poly-Glu,Tyr (Claims 16-31) and a method for preventing or inhibiting neuronal degeneration (Claims 1-9 and 14-15) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the poly-Glu,Tyr can be used to isolate receptors in a biochemical assay.

3. Claims 10-13 and 16-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected material, there being no allowable generic or linking claim. Claims 1-9 and 14-15 will be examined to the extent that they read on a method of treating glaucoma via administration of poly-Glu,Tyr peptide.

***Status of Application, Amendments, and/or Claims***

4. Claims 10-13 and 16-21 are withdrawn from consideration as discussed above and claims 1-9 and 14-15 are under examination.

5. To aid in correlating any papers for this application, all correspondence regarding this application should be directed to Art Unit 1647, Examiner Christopher Nichols.

***Specification***

6. The Specification is objected to because of the following informalities: delete "etc." (pp. 18 line 36, pp. 19 line 28, 30); delete pp. 37 (blank). Appropriate correction is required.

***Drawings***

7. The drawings are objected to because the Y-axis on Figure 1 is not legible nor is the X- or Y-axis on Figure 3. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

***Claim Objections***

8. Claims 1-9 and 14-15 are objected to because of the following informalities: the claims refer to non-elected material. Appropriate correction is required.

9. Claims 1-9 and 14-15 are objected to because of the following informalities: the claims refer to non-elected species. Appropriate correction is required.

10. Claim 14 is objected to because of the following informalities: claim 14 does not end with a period. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-9 and 14-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of lessening retinal ganglion cell (RGC) death via prophylactic administration of pEY, does not reasonably provide enablement for preventing or inhibiting neuronal degeneration, promoting nerve regeneration, or protecting central nervous system (CNS) or peripheral nervous system (PNS) cells from glutamate toxicity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Claims 1-9 are drawn to a method for preventing or treating glaucoma wherein an effective amount of pEY is administered to induce a critical T-cell response in the patient.

12. The specification teaches that activated T-cells that recognize an antigen of the nervous system of the patient can confer neuroprotection. For instance, T-cells specific for myelin basic

protein (MBP) has been shown to be neuroprotective in rat models of partially crushed optic nerve. The specification also teaches that administration of pEY before RGC death due to intraocular pressure induced by glutamate will lessen the degree of RGC loss in a mouse model of glaucoma.

13. The art teaches that administration of COP-1 (synthetic co-polymer) increased retinal ganglion cell (RGC) survival in a glutamate induced mouse model of glaucoma (Schori et al., 2001). In addition, the art teaches that retinal ganglion cell (RGC) death is a hallmark of several ophthalmic diseases including glaucoma, retinal ischemia, anterior ischemic optic neuropathy and optic nerve trauma (Sucher et al., 1997).

14. While general guidance is provided regarding administering pEY to lessen glutamate induced death of retinal ganglion cells, no working examples are provided re: preventing or inhibiting neuronal degeneration, promoting nerve regeneration, or protecting CNS cells from glutamate toxicity.

15. Thus the claimed invention, in that it is directed to a method of treating preventing or inhibiting neuronal degeneration, promoting nerve regeneration (in the CNS or PNS), or protecting CNS cells from glutamate toxicity comprising administering a therapeutically effective amount of pEY which stimulates a critical T-cell response, is not supported by the teachings of the prior art or the specification's disclosure. Therefore, one skilled in this art would be expected to reasonably doubt that the claimed method would work due to the following obstacles: Specific biological actions/activities that the critical T-cell response would effect; How does the pEY peptide effect cells or subjects; Expectation of the critical T-cell response to alleviate glutamate toxicity related pathologies; Expectation of pEY to elicit an immune

response; Expectation of any given pEY T-cell response to be specific, long-lasting, and salubrious. The specification does not provide guidance on how to overcome expected obstacles. The scope of patent protection sought by Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure provided by the specification and prior art for the following reasons.

16. Regarding preventing or inhibiting neuronal degeneration, promoting nerve regeneration, and protecting CNS cells from glutamate toxicity, the art recognizes that stimulation of the immune system as a means of therapy, especially T-cell activation, runs the risk of triggering an autoimmune response. Also, it is not clear whether an elicited T-cell-dependent protective response ameliorates the potential damage or whether the immune response acts in a limited local manner versus a more global, systematic mechanism [Schori et al. (2001); pp. 203 1st col. 4th para.2nd col. 1st para.]. Further, Fisher et al. (2001) teaches that the mechanisms governing the neuroprotection of limited autoimmune T-cell response in nerve damage are not well understood (pp. 141 1st and 2nd column, last and first sentences respectively). Fisher et al. (2001) also notes that it is not clear whether accumulated T-cells in a CNS injury are beneficial or destructive (pp. 141 end of 1st column). In addition, the specification does not show the revival or regeneration of dead neuronal cells. Due to the large quantity of experimentation necessary to test all the possible outcomes of T-cell activation therapy on the nervous system, the lack of direction/guidance presented in the specification regarding evaluating preventing, inhibiting neuronal damage or reviving dead and dying nervous system cells, the absence of working examples directed to all applicable forms of glutamate toxicity, the complex nature of the invention, the unpredictability of the effects of pEY immunization nervous system tissues

(Sucher et al., 1997; Schori et al., 2001; Fisher et al, 2001) and the breadth of the claims which fail to recite limitations for preventing, inhibiting damage or inducing regeneration of nervous tissue, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope. In addition, "prevention" is understood in the art to mean a total protection from disease or injury (Stedman's Medical Dictionary). Thus, given the high level of required effect, a high level of evidence showing prevention is also required. While the specification demonstrates a level of protection of retinal ganglion cells, total prevention was not achieved.

17. Regarding critical T-cell response, the art recognizes that it is not clear what antigen triggers T-cell mediated protection from oxidative stress and glutamate toxicity (Schori et al., 2001). In addition, Cady et al. (2000) teaches the random heterocopolymers of glutamic acid and tyrosine (pEY) trigger strong immune responses only in certain mouse strains. In addition, $pE^{50}Y^{50}$ only stimulated polyclonal proliferation of normal γδ but not αβ T cells (pp. 1790 Abstract). Taken together, this draws into question whether the claimed method of using pEY will evoke any immune response, and if so, a sufficient and appropriate immune response. Due to the large quantity of experimentation necessary to test all the possible immune response to pEY administration, the lack of direction/guidance presented in the specification regarding evaluating the elicited immune responses, both specific and non-specific, the absence of working examples directed to all possible immune responses to pEY, the complex nature of the invention, the unpredictability of the effects of T-cell response on animals, including humans (Vidovic et el., 1985; Schori et al., 2001) and the breadth of the claims which fail to recite limitations for a

critical T-cell response is, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

18. Finally, the application must establish a nexus between the critical T-cell response recited in the claims and treatment of glaucoma as recited in the preamble. In this case, the skilled artisan is not guided as to how pEY must affect one or more activates of glutamate toxicity related neurodegenerative pathologies such that the pEY would be determined to be one that treats neurodegenerative pathologies. Also, T-cell interactions involves several steps and neurodegenerative pathologies covers a myriad of disorders, diseases, and injuries (see discussion and references above) and it is not clear that pEY response (if any) is involved in a rate-limiting step for any of the various steps or disorders such that it could be used to prevent or inhibit damage or injury to the nervous system or regenerate neuronal cells.

***Summary***

19. Claims 1-9 and 14-15 are hereby rejected.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher J. Nichols whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Elizabeth C. Kemmerer

CJN
December 26th, 2002

ELIZABETH KEMMERER
PRIMARY EXAMINER